

Remarks

Applicants acknowledge that the Examiner indicated that claims 1-19, 37, 61, 63, 65, 67, 101, 103, 104, 106, 108, 111, 127, 138, and 147-163 are pending. Applicants also acknowledge that claims 1-19 and 147-163 are currently under consideration. Claims 1 and 19 are hereby amended. No claims are canceled. No new claims are presented. No new matter is introduced.

Applicants further acknowledge that the Examiner indicated that the previous objections to the drawings and the specification have been withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner indicated that claims 1-19, 147-153, and 155-163 remain rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, albeit for apparently new reasons.

Applicants respectfully disagree, and, for reasons set forth below, request the Examiner to withdraw his rejection of claims 1-19, 147-153, and 155-163 under 35 U.S.C. § 112, second paragraph.

The Examiner alleged that claims 1 and 19 are unclear as to whether or not repeating charge motifs are or are not the "repeating units" in view of dependent claims. In the hope of making the following explanation more accessible to the Examiner, let it be understood at the outset that "repeating charge motif" and "repeating unit" are not synonymous terms, although in certain embodiments they may coincide. As discussed in response to the rejection of claims 3 and 4 in the previous office action, the repeating charge motifs can, but need not necessarily, be repeating units within the meaning of those terms as defined at pages 20-21 in the specification. The Examiner will appreciate from reading this portion of the specification that units refer generally to chemical building blocks of various types of polymers, e.g., as occur in nature. Thus for example one type of unit can be an amino acid. As further disclosed at pages 20-21 in the specification, a repeating unit refers to a set of units, said set occurring at least twice in the polymer. For example, a repeating unit could be a set of 10 amino acids. If the set of 10 amino acids is identically reproduced at least once in the polymer, the polymer has identical repeating units. Alternatively, if the set of 10 amino acids occurs more than once in the polymer but the sets of 10 amino acids are non-identical in amino acid composition or sequence, then the repeating units are non-identical. As should be clear from these examples, the repeating charge

motif can reside in either repeating or non-repeating units, and, furthermore, repeating units can be either identical or non-identical.

In view of the foregoing, Applicants assert that the terms “repeating charge motifs” and “repeating units” have definite meaning as provided by the specification. Therefore claims 1 and 19 are not unclear as to whether or not repeating charge motifs are or are not the “repeating units” in view of dependent claims.

The Examiner alleged that claim 2 is unclear as to whether or not the non-repeating units refer to the “repeating charge motifs” as compared to the intervening sequence or whether or not the “non-repeating units” refer to different amino acid residues in a particular sequence. In light of the exemplification provided in the paragraph above, it should be clear that “non-repeating units” can in one embodiment refer to different amino acid residues in a particular sequence. The repeating charge motif can reside within the non-repeating units by, for example, preserving the position of the positively charged amino moiety relative to the negative charge while changing the identity of the particular amino acid carrying the negative charge of the repeating charge motif. Applicants therefore assert that the claim language of claim 2 is not unclear.

The Examiner alleged that claim 3 does not further define how the repeating units are differently placed or how they differ in number compared to claim 1. In response, Applicants assert that it is not necessary further to define how the repeating units are differently placed or how they differ in number compared to claim 1. As should be clear from reading claims 1-3, claim 1 encompasses polymers having non-repeating units and also polymers having repeating units. Claim 3 merely imposes a limitation on claim 1 so as to read only on polymers having repeating units.

The Examiner alleged that claim 4 is unclear as to “identical repeating units” because as written in claims 1 and 4, there can be the “two repeating charge motifs”. This claim rejection has been addressed above.

The Examiner alleged that claims 3-4 and 148-149 are indefinite as to whether or not the recited repeating unit is the same as the repeating unit set forth in claims 1 and 19, respectively. As explained above, because the repeating units can be distinct from the repeating charge motifs, the limitations recited in claims 3-4 and 148-149 do in fact further limit claims 1 and 19, respectively.

The Examiner alleged claim 5 is indefinite because non-identical repeating units would suggest the units are not the same and therefore are not repeats. As explained above, repeating units can be repeating sets of individual units, the composition or order of which can be identical or non-identical. For example, the repeating units can be repeats of sets of 10 amino acids; if the composition or order of individual amino acids differ between sets, then the repeating units, although not identical, are nonetheless repeats of 10-amino acid units. Thus, claim 5 is not indefinite.

The Examiner alleged that recitation of the term "mixed polymer" in claim 6 renders that claim indefinite because only one polymer is recited in claim 1. Claim 6 provides that the polymer of claim 1 is a mixed polymer. The term "mixed polymer" is defined in the specification at page 19, line 25, as a polymer that is heterogeneous in backbone composition. In one embodiment a mixed polymer can mean a peptide-nucleic acid polymer as recited in claim 7. The term "mixed polymer" thus does not render claim 6 indefinite.

The Examiner alleged that claim 15 is unclear as to how native would differ from the claim recitation of non-native. Applicants respectfully submit that native and non-native are unambiguously distinct on their face. By way of example, at page 7, line 13 of the specification, a non-native polypeptide is disclosed as having at least one modified, i.e., non-native, amino acid. The term "non-native" thus does not render claim 15 unclear.

Applicants believe the arguments above fully address the claim rejections under 35 U.S.C. § 112, second paragraph. In view of the foregoing, Applicants respectfully request the Examiner to withdraw his rejection of claims 1-19, 147-153, and 155-163 under 35 U.S.C. § 112, second paragraph.

New Rejections Under 35 U.S.C. § 102(b)

The Examiner indicated that claims 1-6, 14-16, 18-19, 147-148, 152-160, and 162-163 are newly rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Pat. No. 5,514,581 to Ferrari et al. The Examiner asserts that the Ferrari reference discloses the polymer that is claimed in claims 1 and 19. The Examiner also asserts that the recitation of "a pharmaceutical composition" in the preamble of claim 1 of the instant application is afforded no patentable weight per se. Applicants respectfully disagree. The Ferrari reference teaches polymers for use

in the manufacture of various non-pharmaceutical articles, including “formed objects, coatings, or other structural or non-structural components including fibers, films, membranes, adhesives, emulsions, and the like” (column 3, lines 9-13). Without meaning to concede the Examiner’s reasoning, and in order to advance prosecution, Applicants in response have amended claims 1 and 19 to make clear that the instantly claimed subject matter is a pharmaceutical composition for administration to a subject. The Ferrari reference does not anticipate the instantly claimed invention because it does not teach pharmaceutical compositions as instantly claimed. The mere observation that portions of the polymer of Ferrari can be arranged so as to be capable of interacting with a solution or combined with organic material does not anticipate the claimed pharmaceutical composition because a solution or organic material is not necessarily a pharmaceutically acceptable carrier. Applicants therefore respectfully request withdrawal of the rejection of claims 1-6, 14-16, 18-19, 147-148, 152-160, and 162-163 under 35 U.S.C. § 102(b).

New Rejections Under 35 U.S.C. § 103(a)

The Examiner indicated that claims 7, 17, and 161 are newly rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Pat. No. 5,514,581 to Ferrari taken with Basu S et al. (1997) *Bioorg Chem* 8:481-8. Applicants respectfully disagree. The Examiner has failed to make a *prima facie* case for rejecting claims 1, 17, and 161 under 35 U.S.C. § 103(a) because the two references offer no suggestion or motivation to make the proposed combination. Instead, the rejection relies on impermissible application of hindsight analysis to arrive at the rejection.

The Ferrari reference teaches polypeptide block copolymers, some of which contain a plurality of intervening segments containing the sequence Arg-Gly-Asp (RGD) interposed between repeating silk-like strand segments. The silk-like strand segments are capable of interacting with one another, providing polymers useful for the manufacture of various non-pharmaceutical articles, including “formed objects, coatings, or other structural or non-structural components including fibers, films, membranes, adhesives, emulsions, and the like” (column 3, lines 9-13). In some embodiments the polymers are designed to incorporate cell-binding sequences such that the polymers are disclosed to be useful as cell attachment substrates and coatings thereof. There is no teaching in Ferrari to suggest the polymers are taken up or internalized by cells.

The Basu reference teaches linear PNA-peptide conjugates formed between peptide nucleic acids (PNA) useful as antisense agents and a peptide useful for targeting a cell receptor to promote cellular uptake of the PNA. The peptide of Basu is a tetramer (Cys-Ser-Lys-Cys) of insulin-like growth factor 1 (IGF1), linked to the PNA through a Gly₄ linker.

There is no suggestion or motivation to combine the teaching of Ferrari with the teaching of Basu because there is no basis in Ferrari to suggest that a linear conjugate formed between a PNA and the polymer of Ferrari would retain the desired structural or functional features of the polymer of Ferrari. Furthermore, there is no suggestion or motivation to combine the teaching of Ferrari with the teaching of Basu because there is no basis in Basu to suggest that a linear conjugate formed between a PNA and the polymer of Ferrari would be useful for targeting a cell receptor to promote cellular uptake of the PNA. Therefore it would not have been obvious, to one of skill in the art at the time the instant invention was made, to combine the teachings of Ferrari and of Basu.

Accordingly, because the Examiner has failed to make a *prima facie* case for the new rejection of claims 1, 17, and 161 under 35 U.S.C. § 103(a), Applicants respectfully request withdrawal of the rejection.

Maintained Rejections Under 35 U.S.C. § 103(a)

The Examiner maintained his previous rejection of claims 1, 6, and 7 under 35 U.S.C. § 103(a) as being obvious over Simmons GC et al. (*Bioorg Med Chem Lett* (1998) 7:3001-6) taken with Basu S et al. (*Bioconjugate Chem* (1997) 8:481-8) and Nielsen PE (*Curr Opin Biotechnol* (1999) 10:71-5). In response, Applicants respectfully disagree and maintain that the Examiner has failed to make a *prima facie* case for the rejection.

In support of his position, the Examiner asserts that the PNA-peptide conjugates of Simmons can form duplexes, relying on the teaching of Basu. According to Basu, PNA-peptides are used as antisense agents and can form heteroduplexes with sequence-specific complementary nucleic acids. There is no suggestion or motivation in Simmons, Basu, or the combination of Simmons with Basu, to use such heteroduplexes as pharmaceutical compositions, as required by instant claim 1. Any additional teaching provided by Nielsen provides only that PNAs can be administered as therapeutics. Thus the combination of the teachings of Simmons, Basu, and

Nielson fails to render obvious the subject matter of instant claims 1, 6, and 7. Therefore, the Examiner has failed to make a *prima facie* case for the prior rejection of claims 1, 6, and 7 under 35 U.S.C. § 103(a).

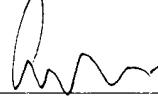
Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1, 6, and 7 under 35 U.S.C. § 103(a).

Summary

Claim amendments and arguments are presented in response to rejections made under 35 U.S.C. § 112, paragraph 2, 35 U.S.C. § 102(b), and 35 U.S.C. § 103(a). The Examiner is urged to withdraw all rejections.

Applicants believe the claims are in condition for allowance. A prompt and favorable action is earnestly solicited.

Respectfully submitted,



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